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14. ABSTRACT
We have discovered that dolphins and killer whales go without any extended periods of sleep and without any behavioral evidence for sleep for more than 1 month after birth. This indicates that any vital functions of sleep can be performed in the waking state, even early in the developmental period, a finding that has important implications for theories of sleep function and control. We have found a marked lateralization of acetylcholine release during unihemispheric sleep. We find that acetylcholine release is maximal in active waking, is significantly lower in quiet waking, does not differ from quiet waking level in REM sleep and is minimal in USWS and BSWS. In the first ever studies of cortical Hcrt release in any animal, we find

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Report Title

CONTINUOUS PERFORMANCE IN THE FUR SEAL: A BRIDGE TO EXTENDED WAKING IN HUMANS FINAL REPORT

ABSTRACT

We have discovered that dolphins and killer whales go without any extended periods of sleep and without any behavioral evidence for sleep for more than 1 month after birth. This indicates that any vital functions of sleep can be performed in the waking state, even early in the developmental period, a finding that has important implications for theories of sleep function and control. We have found a marked lateralization of acetylcholine release during unihemispheric sleep. We find that acetylcholine release is maximal in active waking, is significantly lower in quiet waking, does not differ from quiet waking level in REM sleep and is minimal in USWS and BSWS. In the first ever studies of cortical Hcrt release in any animal, we find evidence for lateralized release of Hcrt, maximal on the waking side of the cortex.

List of papers submitted or published that acknowledge ARO support during this reporting period. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

Lyamin, O.I., Mukhametov, L.M., Siegel,J.M. Relationship between sleep and eye state in Cetaceans and Pinnipeds (Festschrift for Michel Jouvet). Arch Ital Biol.142:557-568 2004.

Zepelin H, Siegel JM, Tobler I Mammalian sleep. In: Principles and Practice of Sleep Medicine (Kryger MH, Roth T, Dement WC eds), pp 91-100, 2005

Lyamin, O., J. Pryaslova, J. Lance, V. and Siegel, J.M. Continuous activity in cetaceans after birth, Nature 435:1177, 2005.

Siegel, J.M. Clues to the functions of mammalian sleep. Nature 437:1264-1271, 2005.

Lyamin OI, Pryaslova J, Lance V, Siegel JM Sleep behaviour: Sleep in continuously active dolphins; Activity and sleep in dolphins (Reply). Nature 441:E11, 2006.

Lyamin O. Lapierre J, Kosenko P , Mukhametov L, Siegel JM EEG asymmetry and spectra power during sleep in the northern fur seal. Physiology and Behavior, (2007, in press).

Lapierre JL, Kosenko PO, Lyamin OI, Kodama, T, Mukhametov LM, Siegel JM Cortical acetylcholine release is lateralized during asymmetrical slow wave sleep in northern fur seals. J. Neuroscience 27:11999-2006 (2007).

Deadwyler S.A., Porrino L., Siegel J.M., Hampson R.E. Systemic and nasal delivery of orexin-a (hypocretin-1) reduces the effects of sleep deprivation on cognitive performance in nonhuman primates J. Neuroscience 2007 (in press)

Number of Papers published in peer-reviewed journals: 8.00

(b) Papers published in non-peer-reviewed journals or in conference proceedings (N/A for none)

Number of Papers published in non peer-reviewed journals:

(c) Presentations

Number of Presentations: 0.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Peer-Reviewed Conference Proceeding publications (other than abstracts):

O. Lyamin, O. V. Shpak, and J. M. Siegel Ontogenesis of rest behavior in killer whales. APSS Meeting, Chicago June 3-8, 2003, Sleep:26 A116, 2003

Symposium to honor Michel Jouvet, Phylogeny and the functions of sleep: clues and challenges from studies of marine mammal sleep Sept 4, 2003.

O.I. Lyamin, L.M. Mukhametov, J.M. Siegel Relationship Between Unihemispheric Sleep and Eye State in Cetaceans and Pinnipeds. Abstracts of the 15th Biennial conference on the biology of Marine Mammals, Greensboro, NC, 14 - 19 December 2003, p. 88-89.

O.I. Lyamin, J.M. Siegel, U.A. Pryaslova, O.V. Shpak Characteristics of the rest-activity cycle in newborn cetaceans (killer whales and bottlenose dolphins) and their mothers. Proceedings of the 7th International Multidisciplinary Conference on Biological Psychiatry □Stress and behavior□, Moscow, Russia, February 26-28, 2003, 111-112
O.I. Lyamin, L.M. Mukhametov, J.M. Siegel Deprivation of Bilateral Sleep Induces EEG Asymmetry In The Fur Seal. 18th meeting of APSS, June 5-10, 2004, Philadelphia. Sleep 27:

O.I. Lyamin, L.M. Mukhametov, J.M. Siegel Association Between EEG Asymmetry And Eye State In Bottlenose Dolphins And Northern Fur Seals. 18th meeting of APSS June 5-10, 2004, Philadelphia. Sleep 27:

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts): 6

(d) Manuscripts

Number of Manuscripts:

Number of Inventions:

Graduate Students

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Faculty Supported

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Under Graduate students supported

NAME	PERCENT SUPPORTED
FTE Equivalent:	
Total Number:	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: .....

The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:.....

The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:.....

Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale): .....

Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering: .....

The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense .....

The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields: .....

Names of Personnel receiving masters degrees

NAME
Total Number:

Names of personnel receiving PHDs

NAME
Total Number:

Names of other research staff

NAME	PERCENT SUPPORTED
FTE Equivalent:	
Total Number:	

Sub Contractors (DD882)

Inventions (DD882)

CONTINUOUS PERFORMANCE IN THE FUR SEAL: A BRIDGE TO EXTENDED WAKING IN HUMANS

PI, Jerome Siegel Ph.D. Co-PI Oleg Lyamin, UCLA, VA GLAHS, Utrish Marine Mammal Research Center

ABSTRACT:

We have discovered that dolphins and killer whales go without any extended periods of sleep and without any behavioral evidence for sleep for more than 1 month after birth. This indicates that any vital functions of sleep can be performed in the waking state, even early in the developmental period, a finding that has important implications for theories of sleep function and control. We have found a marked lateralization of acetylcholine release during unihemispheric sleep. We find that acetylcholine release is maximal in active waking, is significantly lower in quiet waking, does not differ from quiet waking level in REM sleep and is minimal in USWS and BSWS. In the first ever studies of cortical Hcrt release in any animal, we find evidence for lateralized release of Hcrt, maximal on the waking side of the cortex.

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Zurich only (development of digital recorder) Hans-Peter Lipp Ph.D., Alexei Vyssotski
Utrish only:
Digital recorder development, EEG spectral analysis, microdialysis
Petr Kosenko (Severtsov Institute, Ph.D. student)
Julia Pryaslova (Severtsov Institute, Ph.D. student)

Assistants
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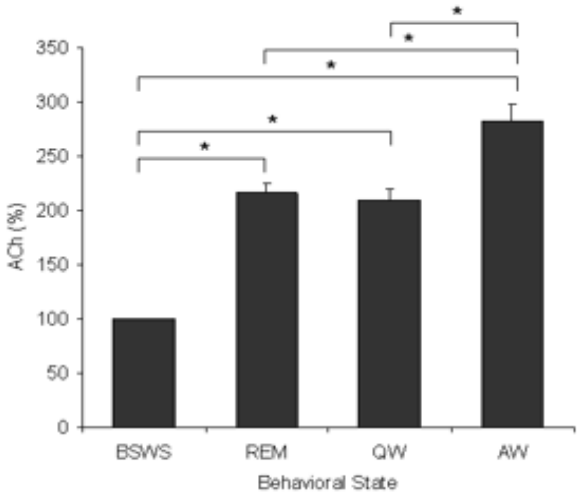
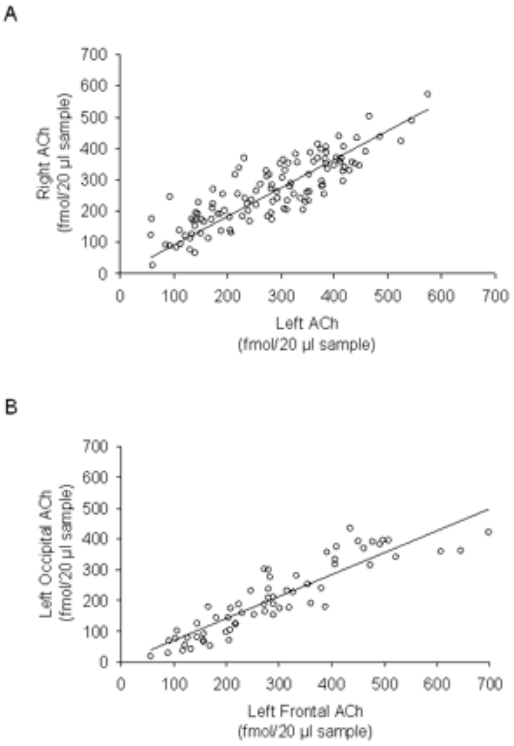
PROGRESS SINCE LAST REPORT

Acetylcholine (Ach) analysis:

Cortical ACh release during bilaterally symmetrical EEG states: Bilateral slow wave sleep (*BSWS), REM sleep, Quiet Waking (QW and Active Waking (AW)*
Mean cortical ACh release was state-dependent ($F_{(3,18)}$=13.89, p<0.0001). ACh levels were minimal during BSWS at 157±35.8 fmol/20 µl sample (n=95), increased to 346±85.8 fmol/20 µl sample (n=38) during REM and to 335±82.7 fmol/20 µl sample (n=150) during QW, and were maximal during AW at 442±109.3 fmol/20 µl sample (n=180). When compared to BSWS, ACh levels increased by 216% during REM, 210% during QW, and 283% during AW as shown in Figure 1. *Post hoc* tests revealed ACh release was: significantly higher during REM, QW, and AW when compared to BSWS

(all *p*-values<0.0001), similar during REM and QW (*p*=0.536), and significantly elevated during AW when compared to REM (*p*=0.020) and QW (*p*=0.007) levels. Changes in cortical ACh release across the sleep-wake cycle are summarized as follows: BSWS<QW=REM<AW. For each pair of symmetrically placed probes, changes in ACh release occurred synchronously in both hemispheres during bilaterally symmetrical states (*i.e.* BSWS, REM, QW, AW) (all *r*-values≥0.810 and all *p*-values<0.0001; Figure 2*A*). For each seal, ACh release occurred in parallel between two sites within the same hemisphere regardless of behavioral state (all *r*-values≥0.722 and all *p*-values<0.0001; Figure 2*B*).





Figures 1 (left) and 2

Cortical ACh release during interhemispherically asymmetrical EEG states: LASWS and RASWS

Three of the 4 fur seals displayed ASWS during the observation period (Seal 1, 2, and 4). For all animals, EEG spectral power in the delta range (1.2-4 Hz) was maximally expressed during BSWS and minimally expressed at a similar level during QW and REM. During LASWS, EEG spectral power was higher in the left hemisphere compared to the right hemisphere (Figure 3*A*). During LASWS, EEG spectral power in the left hemisphere approached but generally did not reach the level observed during BSWS while EEG spectral power in the right hemisphere approached but was typically greater than that observed for QW (Figure 3*A*). The maximal difference in spectral power between hemispheres was not obtained because most sleep displaying interhemispheric EEG asymmetry was not USWS (*i.e.* high-voltage synchronized EEG in one hemisphere and desynchronized EEG in the other). Similar trends, albeit in the opposite hemispheres, were observed during RASWS (Figure 3*A*). For all animals, ACh release was lateralized during ASWS with maximal release in the hemisphere displaying low-voltage activity (*i.e.* higher spectral power) (Figure 3B)

Hypocretin release

We have successfully collected and analyzed our first bilateral hypocretin samples. This required surmounting several hurdles including using new dialysis membranes, transporting samples back to Los Angeles for analysis in good condition and achieving reliable radioimmunoassay measurements. The figures below (figs 4 & 5) show the results of our initial analysis, which indicate lateralization of hypocretin release with USWS.

In combination with our prior results, these data indicate that both hypocretin and acetylcholine are increased in accordance with cortical activation. Our preliminary analysis suggests that the pattern of Hcrt release differs from Ach release in that Hcrt release does not differ between QW and SWS, whereas Ach release is significantly lower in SWS than in QW. It remains to be seen if this is the case for other neurotransmitters implicated in arousal, especially norepinephrine and serotonin.

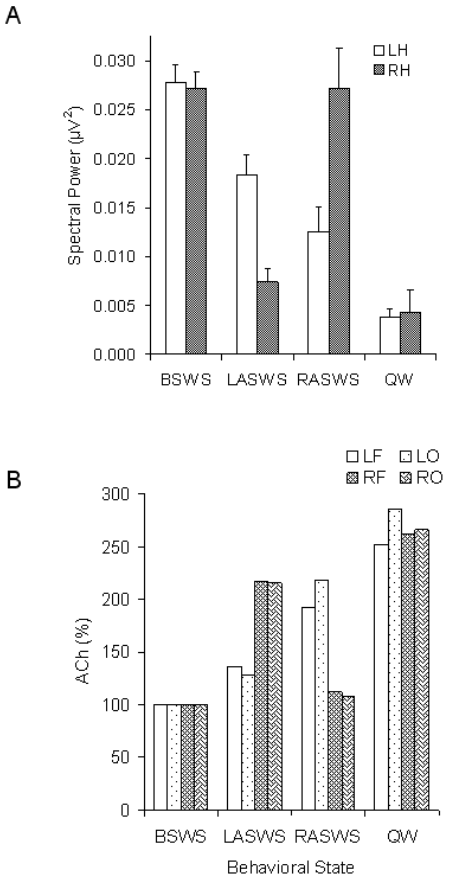


Figure 3

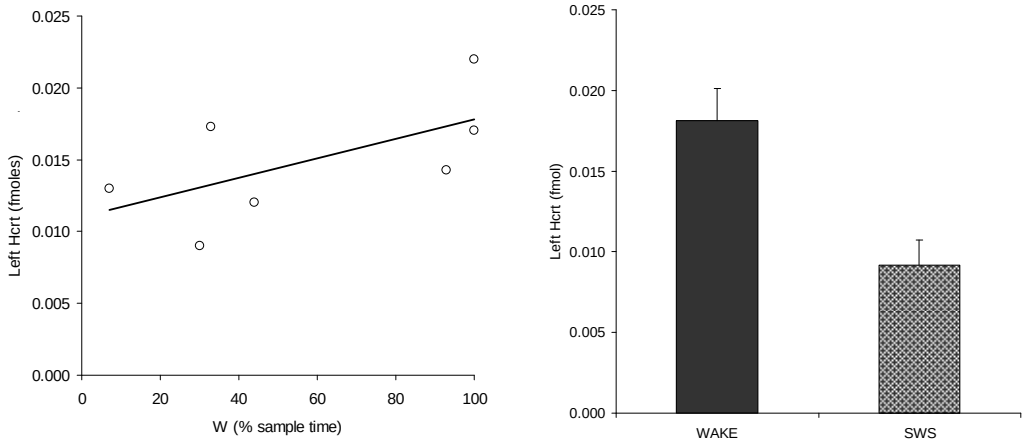
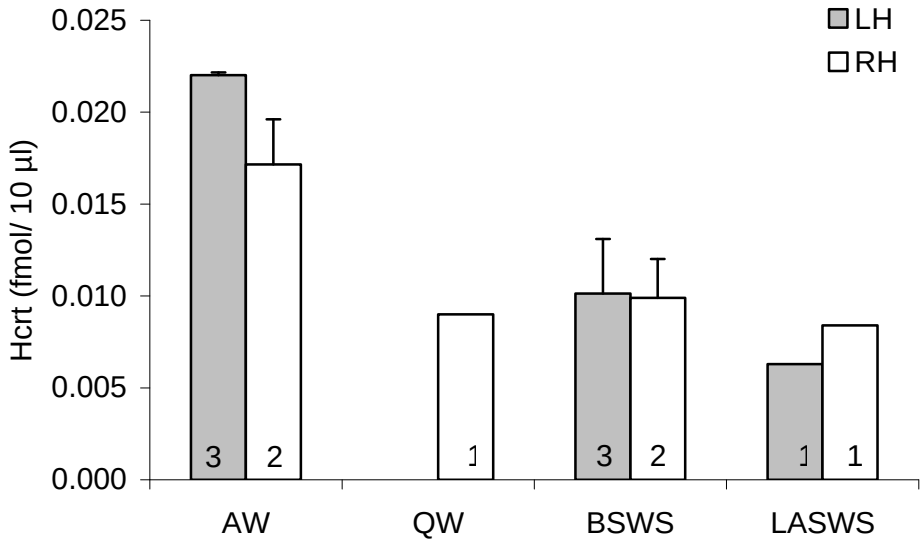


Fig. 4

Fig. 5



Cortical hypocretin release (mean ±SD) was maximal during active wake (AW); the average release for the left and right hemisphere (LH and RH, respectively) combined was 0.020 ±0.003 fmol/10 µl. During bilateral slow wave sleep (BSWS) cortical hypocretin release decreased (0.010 ±0.002 fmol/10 µl) and was significantly less than that of AW (t_8=5.973, p<0.0001). Numbers within each bar represent *n*. Data were obtained from a single northern fur seal (seal 7-06).

In conclusion we have found the following:

1. Cetaceans are able to go without any sustained periods of sleep for several weeks without any adverse consequences. Indeed this is a normal feature of birth and nurturing by the mother. This is the first document instance of a mammal going without sleep for sustained periods (Lyamin et al., 2005;Lyamin et al., 2006;Lyamin et al., 2007).
2, Cetacean sleep may have evolved to allow continuous vigilance as well as to facilitate thermoregulation. Cetacean sleep has been accompanied by anatomical changes in the structure of the hypocretin system and of the suprachiasmatic nucleus.
3. Fur seals can have unihemispheric sleep on land if disturbed. This substitutes for bilateral sleep, such that there is no rebound sleep (in preparation).
4. Unihemispheric slow waves in fur seals and cetaceans is linked to unilateral eyelid closure (Lyamin et al., 2004;Lyamin et al., 2002).
5. Acetylcholine and hypocretin are released in the waking hemisphere at significantly higher rates than in the sleeping hemisphere of fur seals (Lapierre et al., 2007)
6. Hypocretin is linked to positive emotions and approach, but not to simple alerting (Siegel, 2004).
7. Sleep is likely to function mainly as an ecological adaptation, rather than fulfilling any universal biological need (Siegel, 2005).

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Lyamin OI, Mukhametov LM, Siegel JM (2004) Relationship between sleep and eye state in Cetaceans and Pinnipeds. Arch Ital Biol 142:557-568.

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